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| EXAMINER | |
|---|---|
| FISHER, ABIGAIL L | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/594,004 | ROMERO ET AL. | |
| | Examiner | Art Unit | |
| | ABIGAIL FISHER | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-15 are pending.

### *Priority*

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on 9/25/06 was considered by the examiner.

### *Specification*

The use of the trademarks AEROSIL 200 (page 3 and examples) and KOLLICOAT (page 4) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

In the instant specification there is no generic terminology accompanying AEROSIL 200. While applicants have attempted to accompany the trademark KOLLICOAT with the generic terminology, page 4 of the instant specification recites a

copolymer of methacrylic acid. However, the specification does not recite what the other monomer of the copolymer is. Appropriate correction is required.

### *Claim Objections*

Claim 7 is objected to because of the following informalities: a space is needed between "to" and "20%" in line 2. Appropriate correction is required.

Claim 14 is objected to because of the following informalities: a space is needed between "of" and "Aerosil®200" in line 2. Appropriate correction is required.

Claim 13 is objected to because of the following informalities: Aerosil is incorrectly spelt as Aerosile. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.**

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as acrylic polymers and polymers of acrylic acid which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim(s) 4 is(are) directed to encompass **derivatives**, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these derivatives meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim. **Note: MPEP 2163.**

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, (Fed. Cir. 1991), makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), further supports this by stating that:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed **derivatives,** regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Circ. 1993) and

Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016, (Fed. Cir. 1991). In Fiddes v. Baird, 30 USPQ2d 1481, 1483, (Bd. Pat. App. & Int. 1993), claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 (Fed. Cir. 1997) held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Furthermore, to the extent that a functional description can meet the requirement for an adequate written description, it can do so only in accordance with PTO guidelines stating that the requirement can be met by disclosing “sufficiently detailed, relevant identifying characteristics,” including “functional characteristics when coupled with a known or disclosed correlation between function and structure.” Univ. of Rochester v. G.D. Searle, 68 USPQ2d 1424, 1432 (DC WNY 2003).

Therefore, only the above chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 3-5 and 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Regarding claim 3-5 and 11-15, the phrase "and the like" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "and the like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

Claims 13 and 14 contains the trademark/trade name AEROSIL 200. When a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirement of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a fumed silica and, accordingly, the identification/description is indefinite.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claims 1-5 and 7-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Maegerlein et al. (US PGPUB No. 20030153608) as evidenced by Azarmi et al. (Int. J. Pharmaceutics, 2002).**

Maegerlein et al. exemplify a tablet (example 8) comprising formulation 1, calcium phosphate, croscarmelose (carboxymethylcellulose) (5 mg), Eudragit RL (8 mg), Aerosil 200 and magnesium stearate. Formulation 1 is present in 50 mg and of that 50 mg 20% is torasemide (as obtained from Table 1 for formulation 1). Therefore, as calculated by the examiner (since the total weight of the formulation of example 8 is 200 mg) the torasemide is present in 5%, Eudragit RL is present in 4% and crosscarmelose is present in 2.5%. The dosage forms are used for peroral administration (paragraph 0037).

As evidenced by Azarmi et al. Eudragit RL is known to be used in preparation of matrix tablets for oral sustained release (page 171, second paragraph).

**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maegerlein et al. (US PGPUB No. 20030153608) as evidenced by Azarmi et al. in view of Pankhania et al.**

**Applicant Claims**

The instant application claims that the matrix-forming polymer is guar gum.

**Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

The teachings of Maegerlein et al. are set forth above. Specifically, Maegerlein et al. exemplify a formulation comprising torasemide with an acrylic polymer. Other polymers taught include xanthan gum and galactomannan (guar gum) (paragraph 0022).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)***

Maegerlein et al. do not exemplify a formulation comprising guar gum. However, this deficiency is cured by Pankhania et al.

Pankhania et al. is directed to sustained release formulations. It is taught that polymers known for possessing sustained release properties include xanthan gum, guar gum, and acrylic resins. It is taught that one can be replaced for another (column 4, lines 8-24).

***Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Maegerlein et al. and Pankhania et al. and replace the exemplify acrylic polymer with guar gum. One of ordinary skill in the art would have been motivated to replace the exemplified acrylic polymer with guar gum as Maegerlein et al. teach that both are suitable and Pankhania et al. teach that both are known polymers for having sustained release properties. Therefore, one of ordinary skill in the art would have been motivated to replace the exemplified acrylic polymer with guar gum as both are taught by Pankhania et al. as functional equivalents in providing a sustained release.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

**Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berner et al. (US PGPUB No. 20030104052) in view of Kaplan (Drugs, 2000).**

**Applicant Claims**

The instant application claims a prolonged release composition containing torasemide and a matrix-forming polymer.

**Determination of the Scope and Content of the Prior Art (MPEP §2141.01)**

Berner et al. is directed to gastric retentive oral dosage form. The invention is a controlled release oral dosage form for the continuous, sustained administration of a pharmacologically active agent to the upper gastrointestinal tract (abstract). It is taught that the polymer used in the dosage form should not release the drug at too rapid a rate so as to result in drug overdose or rapid passage into and through the upper gastrointestinal tract (paragraph 0062). Suitable polymers taught include cellulosic polymers such as hydroxypropyl methylcellulose (paragraph 0066 and 085), acrylic acid and methacrylic acid polymers (paragraph 0067) and naturally occurring polymers such as guar gum (paragraph 0089). It is taught that the amount of polymer relative to the drug can vary depending on the drug release rate desired and the polymer, its molecular weight and excipient that may be present (paragraph 0096). Active agents include diuretic agent such as torsemide (paragraph 0119). The amount of drug ranges from 0.01 to 80% (paragraph 0133). Tablets prepared for oral administration will generally contain other materials such as binders, lubricants, disintegrants, fillers, etc. Suitable binders include starch and sugars such as lactose. Lubricants include

magnesium stearate. Fillers include materials such as talc and mannitol (paragraph 0137).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims**
***(MPEP §2141.012)***

While Berner et al. teach that a drug that can be administered is torasemide, Berner et al. do not exemplify a formulation comprising torasemide. However, this deficiency is cured by Kaplan.

Kaplan is directed to a review of diuretics as a basis of anti-hypertensive therapy. It is taught that to be effective the diuretic must have activity throughout the day when sodium is ingested in order to maintain a slight degree of contraction of the effective circulating fluid volume (paragraph bridging pages 21-22). Torasemide is recommended as a longer-acting diuretic (page 23, right column, firs complete paragraph). It is taught that long-acting formulations are preferred over short acting agent as there is better adherence with once-daily dosing, fewer tablets incur lower cost, control of hypertension is persistent and smooth rather than intermittent and protection is provided against whatever risk for sudden death, hear attach and stroke that is due to the abrupt increase blood pressure after arising from overnight sleep (page 23, right column, first paragraph of section 3).

***Finding of Prima Facie Obviousness Rationale and Motivation***
***(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Berner et al. and Kaplan and utilize torasemide as the active agent. One of ordinary skill in the art would have been

motivated to utilize torasemide as Berner et al. teach it is a suitable drug and Kaplan teaches that torasemide is a recommended longer-acting diuretic as well as long-acting formulations are preferred over short-acting for many reasons including that control of hypertension is persistent and smooth and protection is provided. Therefore, one of ordinary skill in the art would have been motivated to utilize torasemide in the controlled release formulation of Berner et al. for the benefits that long-acting formulations provide as taught by Kaplan.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Berner et al. and Kaplan and utilize polymers such as acrylic acid polymers, cellulose polymer like hydroxypropyl methylcellulose and guar gum as the polymer for providing sustained release. One of ordinary skill in the art would have been motivated to utilize these polymers as all are taught by Berner et al. as suitable for providing the sustained release of the active agent. It would have been obvious to one of ordinary skill in the art to try any of the swellable bioerodible polymers taught by Berner et al. as a person with ordinary skill has good reason to pursue known options within his or her technical grasp. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Berner et al. and Kaplan and utilize conventional additives when formulating tablets for oral administration. One of ordinary skill in the art would have been motivated to add conventional additives such as

lubricants like magnesium stearate, fillers such as talc or mannitol and binders such as lactose. Berner et al. teach that all of these additives for the formulation of tablets. Therefore, all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

Regarding the claimed amount of toresmide, Berner et al. teach an amount of drug that overlaps that instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Regarding the claimed amount of polymer, Berner et al. that the amount of polymer relative to the drug can vary depending on the drug release rate desired and the polymer, its molecular weight and excipient that may be present. Therefore, the amount of polymer in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. It would have been obvious to one of ordinary skill in the art to vary the amount of polymer in order to manipulate the release rate as taught by Berner et al. It would have been obvious to one of ordinary skill in the art at the time of

the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

## ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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